We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800
Open access books available

122,000
International authors and editors

135M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS BOOK CITATION INDEX INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

4

Epileptic Encephalopathy Syndromes in Infancy

Raidah Albaradie
Dammam University and King Fahd Specialist Hospital-Dammam
Saudi Arabia

1. Introduction

A diagnostic scheme for people with epileptic seizures and with epilepsy proposed by ILAE Commission (2001) (Engel, Jr. et al, 2001) newly adopted the concept of "epileptic encephalopathy" as one of new key terms. It is defined as a condition in which epileptiform abnormalities are believed to contribute to the progressive disturbance in cerebral function, but this definition may be ambiguous.

The proposal include 8 syndromes; early myoclonic encephalopathy, Ohtahara syndrome, West syndrome, Dravet syndrome, myoclonic status in non-progressive encephalopathies, Lennox-Gastaut syndrome, Landau-Kleffner syndrome, epilepsy with continuous spike-waves during slow-wave sleep. To these syndromes, the migrating partial seizures in infancy and severe epilepsy with multiple independent spike foci (Yamatogi et al, 2006) may be reasonably added. In this chapter, we will concentrate on the epileptic encephalopathies that occur only in infancy.

Earlier-onset epilepsy may potentially have a greater impact on a child's development than later-onset epilepsy. Age of epilepsy onset also varies and depends upon the underlying etiology. Seizures and cognitive function may vary over time, depending on the developmental stage of the child. Seizures may eventually remit in many children over time, but behavioral and cognitive problems may persist into adulthood.

"Catastrophic epilepsy" is also a collective term for types of childhood epilepsy that take a highly unfavorable course despite intensive treatment, often with polypharmacy (Kramer, 2005). This is understood almost synonymous with epileptic encephalopathy.

A common feature is that these disorders are usually refractory to standard antiepileptic drugs (AEDs). As a result, more aggressive use of AEDs considered effective in suppressing interictal epileptiform discharges (eg benzodiazepines, valproic acid, lamotrigine), immunomodulatory therapies (eg, corticosteroids, intravenous immunoglobulin [IVIG], plasmapheresis), ketogenic diet, and surgical options are often considered

In this review, epileptic encephalopathies will be dealt in the following concept: a particular group of usually age-related and extremely intractable epilepsies with characteristic generalized minor seizures and massive epileptic EEG abnormalities, both of which cause stagnation/deterioration in mental and cognitive functions in addition to the pre-existing developmental deficit due to organic brain damage.

2. Pathophysiology

The underlying mechanisms of these disorders are still poorly understood. Identifiable factors that may influence the course and degree of cognitive and behavioral impairment in

these disorders includes underlying etiology, age of onset of epilepsy, seizure frequency and severity, interictal epileptiform activity severity, treatment-related adverse effects, cumulative detrimental effects of severe chronic epilepsy, and genetic factors.It remains unclear how much electrical dysfunction contributes to the neuropsychological impairments seen in these disorders. In 1957, Landau and Kleffner suggested that "persistent convulsive discharges in brain tissue largely concerned with language communication" may be responsible for the deficits seen in LKS. This represents the basic concept that frequent seizures and/or interictal discharges may significantly disrupt the function of neuronal networks involved in language, learning, memory, behavioral regulation, and other higher cortical functions, resulting in either transient or permanent deficits. For example, continuous abnormal discharges during sleep may cause disruption of hippocampal function and interfere with learning and memory while awake and memory consolidation in sleep (Coppola G, 1995. Moruzzi G, 1995).

The duration of electrical dysfunction may in part determine the severity of the disorder. Impairment at the exact moment of an interictal discharge has been described and is termed transient cognitive impairment (Shewmon DA, 1989. Shewmon DA, 1988. Kasteleijn-Nolst, 1995. Aarts JH, 1989. Binnie, 2003. Binnie, 1993. Binnie, 1987). Although challenging to demonstrate, this appears to be due to a temporary disruption of a cortical network involved in a particular function at the time of an interictal epileptiform discharge.

3. Genetics

The epileptic encephalopathies of infancy and childhood are a collection of epilepsy disorders characterized by refractory, severe seizures and poor neurological outcome, in which the mechanism of disease is poorly understood.

There are only some reported cases where the disease locus were identified such as, a disease locus at chromosome 2q35-37, which enabled identification of the causative mutation in the gene SLC19A3 in four Japanese patients in a Japanese pedigree who presented with epileptic spasms in early infancy, severe psychomotor retardation, and characteristic brain MRI findings of progressive brain atrophy and bilateral thalami and basal ganglia lesions (Yamada, 2010). In a recent report, the clinical presentation and evolution of epileptic encephalopathy in a patient, associated with a loss-of-function mutation in the phospholipase C-β 1gene. The discovery of a phospholipase C-β 1 mutation allows us to propose a novel potential underlying mechanism in early-onset epileptic encephalopathy (Kurian, 2010).

A genetic variants in the MC4R promoter are associated with the development of infantile spasms. The rs11872992 polymorphism influences ACTH treatment responses in patients with infantile spasms (Liu ZL, 2007).

4. Epileptic encephalopathy syndromes in infancy

4.1 Early infantile epileptic encephalopathy (Ohtahara syndrome)

Ohtahara Syndrome is the earliest form of the age dependant neo-natal epileptic encephalopathies and was first described by Dr. Ohtahara and colleagues in 1976. It is often defined as "Early Infantile Epileptic Encephalopathy (EIEE) with Burst-Suppression" or "Early Myoclonic Encephalopathy (EME)" (Aicardi, 2002. Clarke, 1987).

Often little is know about the exact causes of Ohtahara, and it is important to remember that it is a syndrome with a definition as opposed to a disease in itself. Although children

suffering from Ohtahara may initially have very similar symptoms, developmental problems and clinical test results, the underlying causes of their illness may differ considerably, and in many cases these causes may never be known (Commission, 1985 &1989).

4.2 Symptoms

- Symptoms appear within the first 3 months of birth and usually within first 10 days. Often symptoms will appear with first few hours after birth, and in some cases mothers have felt possible seizures activity in utero. Onset is acute is previously normal children (Donat, 1992. du Plessis, 1993).
- Initial symptoms include poor suck reflex and general floppiness, followed by epileptic seizures.
- Main seizure pattern is tonic spasms; Other patterns include tonic/clonic, clonic, myoclonic, atonic, absences, partial, complex partial (with or without secondary generalisation), gelastics and Jacksonians. Seizures can appear in clusters or singly and patterns are likely to change with time. It is not uncommon for patterns to reappear at a later stage (Donat, 1992. Engel, 2001).
- EEG pattern is characterised as Burst-Suppression during both waking and sleeping states. This means the EEG (electroencephalogram) tends to show periods of very little electrical brain activity followed by a burst of high spiky activity before returning to very low activity again. Sometimes, one side of the brain seems to be affected more than the other (Fusco, 2001).
- Seizures are intractable, although in some cases can be improved through with treatment (Komaki,1999).
- Further symptoms may include breathing difficulties, apnoeas, poor swallow reflex and reflux. In some cases these can further give rise to other complications such as chest infections (Donat, 1992).
- OS thought to be a progressive, neuro-degenerative disorder with increasing frequency of seizures and with severe retardation of psychomotor development and learning difficulties (Miller, 1998).
- This deterioration may slow with time, although setbacks should be expected along the way. Development skills can be assessed after approximately ten months of age (Murakami, 1993 & Ogihara, 1993).
- Some research has shown boys can be affected more than girls.

4.3 Prognosis

- Prognosis is poor with severe psychomotor retardation and significant learning difficulties.
- The seizures are very often intractable and resistant to antiepileptic therapy making control difficult.
- Frequently cases will progress to West syndrome or partial epilepsy (usually during infancy). Later a much smaller number progress to Lennox-Gastaut syndrome. Psychomotor development may be slightly better if the infants do not develop West or Lennox-Gastaut syndrome
- Half of the children are likely to die in infancy or childhood.
- Some children who survive early children will often see a general improvement beyond initial expectations and increased life expectancy (Murakami, 1993 & Ogihara, 1993).

4.4 Etiology

Research has shown many different causes (polyetiology), however most are linked to some form malformative pathologies (structural brain damage). In most children there has been a significant underdevelopment of part or indeed all of the cerebral hemispheres. After some months Magnetic Resonance Imaging (MRI) can be used to detect such structural malformations.

Very occasionally, babies may suffer from a metabolic disorder where an important part of the body's biochemistry is affected. To rule out this possibility, doctors will carry out a number of specialised metabolic tests, and in most cases no abnormalities will be found. If, however, a metabolic disorder is discovered (at which point the Ohtahara diagnosis will be replaced), the geneticist will discuss a course of potential treatments. At times, in spite of adequate treatment, babies with metabolic diseases can deteriorate (Komaki, 1999, Murakami, 1993, Tominaga, 1993, Williams, 1998).

4.5 Treatments

Although the disorder in incurable, much can be done to improve the lives not only of the children but also the families. Seizure control is the main aim and will be attempted either through optimised dosages of anticonvulsants such as Vigabattrin (Topamax), Dillantin, Zonegran, Phenobarbitone, or through steroid therapies using ACTH and Prednisone. Anticonvulsants or AIDS (AED's antiepileptic drugs) can be taken in either mono or poly therapies. The quest for seizure control can be a slow and frustrating process.

There is also the possibility of utilizing such treatments as the Ketogenic Diet, the VNS (link) or more invasive surgery, such as a partial resection or complete hemispherectomy.

Physiotherapy and Occupational Therapies can help improve motor skills, while Hippotherapy can help improve general mobility, strength and endurance (Komaki, 1999, Ohno, 2000 & Pedespan, 1995).

5. Risk of reoccurrence in future pregnancies

Due to lack of research it is hard for specialists to give an accurate risk of reoccurrence in future pregnancies. However many doctors will site an approximate figure of 5% although this appears to be based on a generic risk for all epileptic disorders. This support group knows of only 4 families around the world with OS siblings, and so this 5% figure is not implausible.

Cases caused by a metabolic disorder will carry a higher risk. Single gene metabolic disorders have a 25% reoccurrence risk. But as mentioned above these cases are rare among Ohtahara children (Donat, 1992).

6. Early myoclonic encephalopathy

Early myoclonic encephalopathy, an epileptic syndrome with onset either in the neonatal period or first months of life, is characterized by erratic, fragmentary, or massive myoclonus, partial seizures, and late tonic spasms. The prognosis is severe. Early myoclonic encephalopathy with the Ohtahara syndrome make the entity of severe neonatal epilepsies with suppression burst pattern.

Since 1978, numerous papers have been published that describe an epileptic syndrome with onset either neonatally or in the first months of life and characterized by erratic,

fragmentary myoclonus, massive myoclonus, partial seizures, late tonic spasms, and EEG signs such as suppression-burst pattern. Various terms have been used: neonatal myoclonic encephalopathy (Aicardi, 1978). In 1989, the ILAE Commission of Classification and Terminology recognized this syndrome with the term "early myoclonic encephalopathy" and classified it under "symptomatic generalized epilepsies and syndromes with non-specific etiology". The same Commission distinguished this syndrome from similar clinical pictures, such as "early infantile epileptic encephalopathy with suppression-burst" or Ohtahara syndrome (Commission on Classification and Terminology of the International League Against Epilepsy, 1989).

6.1 Symptoms

Early myoclonic encephalopathy is characterized clinically by the onset of erratic or fragmentary myoclonus. Other types of seizures, including simple partial seizures, massive myoclonia, and tonic spasms can also occur. Erratic, partial myoclonus usually appears as the first seizure, even as early as a few hours after birth. The myoclonus usually involves the face or extremities and may be restricted to an eyebrow, a single limb, or a finger. The jerks occur when infants are awake or asleep, and they are often described as "erratic" because they shift typically from one part of the body to another in a random, asynchronous fashion. Frequency varies from occasional to almost continuous. In addition to limited partial myoclonus, generalized myoclonus may also be observed occasionally in some cases. Partial seizures are frequent and occur shortly after erratic myoclonus. The semiology of partial seizures is subtle, consisting, for instance, of eye deviation or autonomic phenomena such as apnea or flushing of the face (Dalla Bernardina, 1983). Tonic seizures are reported frequently and can occur in the first month of life or afterwards; they may occur both in sleep and wakefulness. From a clinical standpoint, the child presents a diffuse tonic contraction, usually extending to the extremities. Real epileptic spasms are rare and generally appear later.

Neurologic abnormalities are constant: very severe delay in psychomotor acquisitions, marked hypotonia, and disturbed alertness, sometimes with vegetative state. Dalla Bernardina and colleagues reported deterioration in the patients, this characteristic is difficult to confirm because the onset of the disease is very early. Signs of peripheral neuropathy may also occur in rare cases (Aicardi, 2002 & Dalla Bernardina, 1983).

6.2 Etiology

No obstetrical complications or other perinatal problems were observed in the reported cases. Consequently, early myoclonic encephalopathy is believed to have various prenatal etiologies that often remain unknown. Siblings have been affected in a few instances (Aicardi, 2002 & Dalla Bernardina, 1983). The parents were believed to be healthy and no consanguinity was recognized. Autosomal recessive inheritance appears likely but has not been proved.

Some conditions, such as inborn error of metabolism, can produce the clinical and EEG picture typical of early myoclonic encephalopathy such as: nonketotic hyperglycinemia, D-glyceric acidemia , propionic acidemia , molybdenum cofactor deficiency, and methylmalonic acidemia . Some reports of patients with a clinical picture of early myoclonic encephalopathy and an atypical suppression-burst pattern, with full recovery after administration of pyridoxine. Some malformative disorders can also cause early myoclonic

encephalopathy, but more often they produce Ohtahara syndrome (Lombroso, 1990, Martin, 1981, Vigevano,2002 & Wang, 1998).

6.3 Pathogenesis and pathophysiology

The lack of consistent neuropathologic features suggests that etiology may vary from case to case. Pathologic findings include a drop-out of cortical neurons and astrocytic proliferation, severe multifocal spongy changes in the white matter, perivascular concentric bodies, demyelination in cerebral hemispheres, imperfect lamination of the deeper cortical layers, and unilateral enlargement of cerebral hemisphere with astrocytic proliferation. On the other hand, absence of pathologic abnormality was reported in 2 affected cases. Others proposed the hypothesis of the presence of numerous large spiny neurons dispersed in the white matter along the axons of the cortical gyri has been interpreted as an abnormal persistence of interstitial cells (Dalla Bernardina, 1983, Aicardi, 1985 & Spreafico, 1993).

6.4 Epidemiology

Early myoclonic encephalopathy is very rare. An epidemiologic study on childhood epilepsy carried out in Okayama Prefecture, Japan, detected 4 cases of early myoclonic encephalopathy (0.168%) among 2378 epileptic patients younger than 10 years of age on the prevalence day of December 31, 1980. The prevalence of early myoclonic encephalopathy was higher than Ohtahara syndrome (0.04%), but much lower than West syndrome (1.68%). Similar results were obtained more recently in the same region (Oka E, 2002).

6.5 Prevention

No information is available. Genetic counseling might be helpful.

6.6 Differential diagnosis

Early myoclonic encephalopathy and Ohtahara syndrome share common clinical and EEG characteristics, such as onset in the first few months of life and suppression-burst pattern on EEG, but there are several features that distinguish these 2 entities.

The presence of erratic myoclonus and the absence of tonic spasms distinguish early myoclonic encephalopathy from Ohtahara syndrome.

In Ohtahara syndrome, the suppression-burst pattern is characterized by longer paroxysmal bursts and shorter periods of suppression. Etiologically, Ohtahara syndrome is mainly due to structural abnormalities; in the early myoclonic encephalopathy case series we found metabolic disorders and a high proportion of cryptogenic cases. The prognosis is more severe in early myoclonic encephalopathy.

The EEG pattern of "burst- suppression" with long suppression periods, without variations between different vigilance stages, distinguishes early myoclonic encephalopathy from other conditions that produce a neonatal "burst-suppression" picture, such as hypoxic-ischemic encephalopathy and neonatal convulsions (Aicardi, 2002 & Ohtahara S, 2003).

6.7 Diagnostic workup

In early myoclonic encephalopathy, EEG is characterized by a "burst-suppression" pattern with bursts of spikes, sharp waves, and slow waves, which are irregularly intermingled and separated by periods of electrical silence. The EEG paroxysms may be either synchronous or asynchronous over both hemispheres. There is no normal background activity. The burst-

suppression pattern usually evolves into atypical hypsarrhythmia or into multifocal paroxysms after 3 to 5 months of life.
Erratic myoclonus does not generally have an ictal EEG counterpart. Partial seizures have EEG characteristics similar to those of neonatal fits. The CT and MR findings vary and are related to etiology. The brain may be either grossly normal or have asymmetrical enlargement of 1 hemisphere, dilatation of the corresponding lateral ventricle, or cortical and periventricular atrophy.
Considering the inborn error of metabolism reported above, the serum levels of amino acids should be determined, especially glycine and glycerol metabolites, and organic acids, as well as the amino acids in the cerebrospinal fluid (Aicardi, 2002).

6.8 Prognosis
The prognosis for early myoclonic encephalopathy is poor. The patients reported either died before 1 or 2 years of life, with a mortality rate of 50% or greater, or survived in a persistent vegetative state. Early myoclonic encephalopathy can persist into childhood or evolve into severe partial epilepsy.

6.9 Management
There is no effective therapy for early myoclonic encephalopathy. Antiepileptic drugs as well as adrenocorticotropic hormone or corticosteroids cannot alter the poor prognosis. In nonketotic hyperglycinemia, pyridoxine and benzoate can normalize the levels of glycine in the blood and improve the EEG picture, but without improvements in prognosis. Trying pyridoxine is always justified in cases of early myoclonic encephalopathy.

6.10 Infantile spasms (West syndrome)
West syndrome usually occurs in the first year of life and consists of the triad of infantile spasms, developmental deterioration, and a hypsarrhthymia pattern on EEG.

6.11 Symptoms
The epileptic spasms are brief, generalized seizures involving extension and/or flexion axially and of the extremities. An individual spasm lasts seconds, often longer than typical myoclonic seizures, though not as long as most tonic seizures. The spasms may be subtle and may be isolated at onset, typically clustering later in the course. Several clusters per day, particularly in drowsiness, are characteristic.

6.12 Diagnosis
Hypsarrhythmia, the typical interictal EEG finding, consists of a disorganized pattern with asynchronous, very high amplitude slowing and frequent multifocal spike and sharp wave discharges. The ictal EEG typically reveals a generalized slow wave followed by diffuse voltage attenuation (electro-decrement), which may associated with a spasm or be only electrographic (without clinical correlate).

6.13 Etiology
No clear etiology is found in approximately 40% of cases (Hrachovy, 2008 & Vigevano, 1992). There is a broad range of potential causes, including cerebral malformations, infection, hemorrhage, hypoxic-ischemic injury, metabolic disorders, and genetic conditions, such as Down syndrome.

6.14 Treatment

- Variation in study methodologies prohibits a clear recommendation for first-linetreatment; however, ACTH and vigabatrin are usually used in practice.
- Corticosteroids may be less efficacious than ACTH, although they are effective. Vigabatrin may be more efficacious in tuberous sclerosis. Other agents that are efficacious include valproate, levetiracetam, topiramate, zonisamide, lamotriginen and benzodiazepines.
- The ketogenic diet is helpful in most cases. Focal cortical resection or hemispherectomy may be considered for cases that are lesional and medically intractable (M.T. Mackay, 2004).

6.15 Prognosis

Development remains unaffected only in a minority. Most children experience slowing, plateauing, or regression of their developmental trajectory. The developmental prognosis partially depends on the etiology. No specific AED has been shown to affect long-term developmental outcome. An extensive literature review revealed that 16% had normal development, and 47% had continued seizures at an average follow-up of 31 months (Hrachovy, 2008). When classified by etiology, normal development was described in 51% of cryptogenic cases versus only 6% of symptomatic cases. Approximately 17% of cases evolved into Lennox-Gastaut syndrome.

7. Malignant epilepsy with migrating partial seizures in infancy

7.1 Symptoms

- Onset of this rare syndrome occurs in the first year of life and may occur in the neonatal period. It is characterized by frequent partial seizures of multifocal onset, with autonomic or motor involvement. The seizures increase in frequency and may become near-continuous.
- Lateral deviation of the head and eyes, lateral eye jerks, fixed sight, clonic twitches of the eyelids, increased tone or clonic jerks of one or both limbs on one side, chewing movements, apnea, flushing of the face, salivation, mastication, secondary tonic-clonic generalization.

7.2 Diagnosis

- The interictal EEG reveals multifocal epileptiform activity and slowing. Diffuse slowing of the background activity. Few patients may have a normal EEG.
- Then the EEG background activity became slow with fluctuating asymmetry between different recordings. Initially sleep-waking cycle can be identified, spindles are rare and asymmetric
- The ictal EEG confirms multifocal onsets, which may shift from seizure to seizure.

7.3 Etiology

In most cases, there is no clear etiology or structural problems, suggesting genetic factors may be causative or contributory.

7.4 Treatment

Seizures are often difficult to control with standard AEDs. Bromides, stiripentol, and clonazepam may be helpful in some cases.

7.5 Prognosis

Developmental regression is common, and death has been reported in infancy and childhood in severe cases (Coppola G, 2009).

8. Myoclonic status in non-progressive encephalopathies

This rarely reported disorder has onset in infancy or early childhood, with onset usually during the first year of life (Dalla Bernardina B, 1999).

8.1 Symptoms

Seizures typically begin with partial motor seizures, although myoclonic status may occur at onset. Myoclonic absences, massive myoclonias, and rarely generalized or hemiclonic seizures may occur. Myoclonias may be multifocal and occur with startles. Myoclonic status epilepticus may be recurrent. Motor abnormalities and movement disorders are common.

8.2 Diagnosis

The interictal EEG consists of multifocal epileptiform discharges and background slowing. Epileptiform discharges are potentiated in sleep, in some cases similar to an ESES pattern. Ictal EEG recording may demonstrate generalized slow spike and wave, or an absence pattern, depending on the seizure type.

8.3 Etiology

A genetic cause is identifiable in approximately half of children, including Angelman syndrome and 4p- syndrome (46). Other reported causes include hypoxic-ischemic injury and cortical dysplasia.

8.4 Treatment

Episodes of myoclonic status may respond to benzodiazepines. AEDs that may be efficacious include valproate with ethosuximide or clobazam.

8.5 Prognosis

Children have a poor prognosis, experiencing developmental regression, and eventual severe mental retardation. The repeated episodes of myoclonic status may contribute to cognitive deterioration (Dalla Bernardina B, 1999)

9. References

Aarts JH, Binnie CD, Smit AM, Wilkins AJ. Selective cognitive impairment during focal and generalized epileptiform EEG activity. *Brain*. Mar 1984;107 (Pt 1):293-308.

Aicardi J, Ohtahara S. Severe neonatal epilepsies with suppression-burst pattern. In: Roger J, Bureau M, Dravet CH, Genton P, Tassinari CA, Wolf P, editors. Epileptic Syndromes in Infancy, Childhood and Adolescence. 3rd ed. London: John Libbey & Company Ltd, 2002:33-44.

Aicardi J. Early myoclonic encephalopathy. In: Roger J, Dravet C, Bureau M, Dreifuss FE, Wolf P, editors. Epileptic syndromes in infancy, childhood and adolescence. London: John Libbey Eurotext, 1985.

Aicardi J, Goutieres F. Encephalopathie myoclonique neonatale. Rev EEG Neurophysiol 1978;8:99 101.

Binnie CD. Cognitive impairment during epileptiform discharges: is it ever justifiable to treat the EEG?. *Lancet Neurol*. Dec 2003;2(12):725-30. Binnie CD. Significance and management of transitory cognitive impairment due to subclinical EEG discharges in children. *Brain Dev*. Jan-Feb 1993;15(1):23-30.

Binnie CD, Kasteleijn-Nolst Trenite DG, Smit AM, Wilkins AJ. Interactions of epileptiform EEG discharges and cognition. *Epilepsy Res*. Jul 1987;1(4):239-45.

Clarke M, Gill J, Noronha M, McKinlay I. Early infantile epileptic encephalopathy with suppression burst: Ohtahara syndrome. Dev Med Child Neurol 1987;29:520-8.

Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia 1989;30:389-99.

Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for classification of epilepsies and epileptic syndromes. Epilepsia 1985;26:268-78.

Coppola G. Malignant migrating partial seizures in infancy: an epilepsy syndrome of unknown etiology. Epilepsia. 2009 May;50 Suppl 5:49-51.

Coppola G, Plouin P, Chiron C, Robain O, Dulac O. Migrating partial seizures in infancy: a malignant disorder with developmental arrest. *Epilepsia*. Oct 1995;36 (10):1017-24.

Dalla Bernardina B, Fontana E, Darra F. Myoclonic status in non-progressive encephalopathies. International Leauge Against Epilepsy. Available at http://www.ilae.org/ctf/myoclon_stat_nonpro_enceph.html. Accessed July 8, 1999.

Dalla Bernardina B, Dulac O, Fejerman N, et al. Early myoclonic epileptic encephalopathy (E.M.E.E.). Eur J Pediatr 1983;140:248-52.

Donat JF. The age-dependent epileptic encephalopathies. J Child Neurol 1992;7:7-21.

du Plessis AJ, Kaufmann WE, Kupsky WJ. Intra-uterine onset myoclonic encephalopathy associated with cerebral cortical dysgenesis. J Child Neurol 1993;8:164-70.

Engel J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: Report of the ILAE Task Force on classification and terminology. Epilepsia 2001;42:796-803.

Engel, Jr. J. ILAE Commission Report. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy. Report of the ILAE Task Force on Classification and Terminology. *Epilepsia* 2001; 42: 796-803.

Fusco L, Pachatz C, Di Capua M, Vigevano F. Video-EEG aspects of early-infantile epileptic encephalopathy with suppression-bursts (Ohtahara syndrome). Brain Dev 2001;23:708-14.

G. Kraemer. Catastrophic epilepsy of childhood. Epilepsy from A to Z. 4th ed. Stuttgart, New York, Thieme, 2005:113Hrachovy RA, Frost JD. Severe Encephalopathic Epilepsy in Infants: Infantile Spasms (West Syndrome). In: Pellock JM, Bourgeois BFD, Dodson WE. *Pediatric Epilepsy*. Third Edition. New York, NY: Demos Medical Publishing; 2008:16.

Kasteleijn-Nolst Trenite DG. Transient cognitive impairment during subclinical epileptiform electroencephalographic discharges. *Semin Pediatr Neurol*. Dec 1995;2(4):246-53.

Komaki H, Sugai K, Sasaki K, et al. Surgical treatment of a case of early infantile epileptic encephalopathy with suppression-bursts associated with focal cortical dysplasia. Epilepsia 1999;40:365-9.Kurian MA, Meyer E, Vassallo G, et al.Phospholipase C beta 1 deficiency is associated with early-onset epileptic encephalopathy. Brain. 2010:133(10):2964-70.

Liu ZL, He B, Fang F, et al: Analysis of single nucleotide polymorphisms in the melanocortin-4 receptor promoter in infantile spasms. Neuropediatrics.2007,38(6):304-9.

Lombroso C. Early myoclonic encephalopathy, early infantile epileptic encephalopathy and benign and severe infantile myoclonic epilepsies: a critical review and personal contributions. J Clin Neurophysiol 1990;7:380-408.

M.T. Mackay, MBBS; S.K. Weiss, et al, (2004). Medical Treatment of Infantile Spasms. *Neurology* 2004;62:1668-1681

Martin HJ, Deroubaix-Tela P, Thelliez P. Encéphalopathie épileptique néonatale à bouffées périodiques. Rev EEG Neurophysiol Clin 1981;11:397-403.

Miller SP, Dilenge ME, Meagher-Villemure K, O'Gorman AM, Shevell MI. Infantile epileptic encephalopathy (Ohtahara syndrome) and migrational disorder. Pediatr Neurol 1998;19(1):50-4.

Moruzzi G, Magoun HW. Brain stem reticular formation and activation of the EEG. 1949. *J Neuropsychiatry Clin Neurosci*. Spring 1995;7(2):251-67.

Murakami N, Ohtsuka Y, Ohtahara S. Early infantile epileptic syndromes with suppression-bursts: early myoclonic encephalopathy vs. Ohtahara syndrome. Jpn J Psychiatry Neurol 1993;47:197-200.

Ogihara M, Kinoue K, Takamiya H, et al. A case of early infantile epileptic encephalopathy (EIEE) with anatomical cerebral asymmetry and myoclonus. Brain Dev 1993;15:133-9.

Oka E. Childhood epilepsy in Okayama Prefecture, Japan: a neuroepidemiological study. No To Hattatsu (Tokyo) 2002;34:95-102.

Ohno M, Shimotsuji Y, Abe J, Shimada M, Tamiya H. Zonisamide treatment of early infantile epileptic encephalopathy. Pediatr Neurol 2000;23:341-4.

Ohtahara S, Yamatogi Y. Epileptic encephalopathies in early infancy with suppression-burst. J Clin Neurophysiol 2003;20:398-407.

Pedespan JM, Loiseau H, Vital A, et al. Surgical treatment of an early epileptic encephalopathy with suppression-bursts and focal cortical dysplasia. Epilepsia 1995;36:37-40.

Tominaga I, Kaihou M, Kimura T, et al. Early infantile epileptic encephalopathy (Ohtahara syndrome) with poly-microgyria. Rev Neurol (Paris) 1993;149(10):532-5.

Shewmon DA, Erwin RJ. Transient impairment of visual perception induced by single interictal occipital spikes. *J Clin Exp Neuropsychol*. Oct 1989;11(5):675-91.

Shewmon DA, Erwin RJ. The effect of focal interictal spikes on perception and reaction time. II. Neuroanatomic specificity. *Electroencephalogr Clin Neurophysiol*. Apr 1988;69(4):338-52.

Spreafico R, Angelini L, Binelli S, et al. Burst suppression and impairment of neocortical ontogenesis: electroclinical and neuropathologic findings in two infants with early myoclonic encephalopathy. Epilepsia 1993;34(5):800-8.

Vigevano F, Bartuli A. Infantile epileptic syndromes and metabolic etiologies. J Child Neurology 2002;17(3):3S9-13.

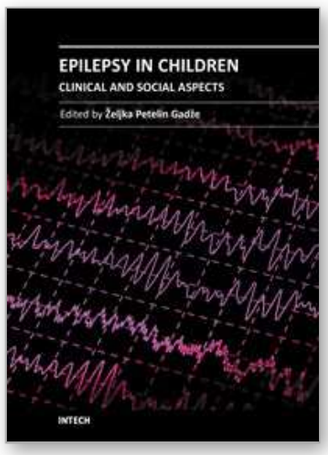
Vigevano F, Fusco L, Cusmai R, Claps D, Ricci S, Milani L. The idiopathic form of West syndrome. Epilepsia 1993;34:743-6

Wang PJ, Lee WT, Hwu C, et al. The controversy regarding diagnostic criteria for early myoclonic encephalopathy. Brain Dev 1998;20:530-5.

Williams AN, Gray RG, Poulton K, et al. A case of Ohtahara syndrome with cytochrome oxidase deficiency. Dev Med Child Neurol 1998;40:568-70.

Yamada K, Miura K, Hara K, et al. A wide spectrum of clinical and brain MRI findings in patients with SLC19A mutations. BMC Med Genet 2010:22;11(1):171.

Yamatogi Y, Ohtahara S. Multiple independent spike foci and epilepsy with special reference to a new epileptic syndrome of "severe epilepsy with multiple independent spike foci". *Epilepsy Res* 2006; 70S: S96-104.



Epilepsy in Children - Clinical and Social Aspects
Edited by Dr. Zeljka Petelin Gadze

ISBN 978-953-307-681-2
Hard cover, 234 pages
Publisher InTech
Published online 15, September, 2011
Published in print edition September, 2011

Epilepsy is a neurological condition that accompanies mankind probably since its inception. About 400 years before Christ, the disease was already known by Hippocrates, who wrote the book â€œOn The Sacred Diseaseâ€. Classically, epilepsy has been defined as a chronic condition characterized by an enduring propensity to generate seizures, which are paroxysmal occurring episodes of abnormal excessive or synchronous neuronal activity in the brain. Out of all brain disorders, epilepsy is the one that offers a unique opportunity to understand normal brain functions as derived from excessive dysfunction of neuronal circuits, because the symptoms of epileptic seizures are not the result of usual loss of function that accompanies many disease that affect the brain. I am therefore extremely honoured to present this book. The 15 very interesting chapters of the book cover various fields in epileptology â€“ they encompass the etiology and pathogenesis of the disease, clinical presentation with special attention to the epileptic syndromes of childhood, principles of medical management, surgical approaches, as well as social aspects of the disease.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:

Raidah Albaradie (2011). Epileptic Encephalopathy Syndromes in Infancy, Epilepsy in Children - Clinical and Social Aspects, Dr. Zeljka Petelin Gadze (Ed.), ISBN: 978-953-307-681-2, InTech, Available from: http://www.intechopen.com/books/epilepsy-in-children-clinical-and-social-aspects/epileptic-encephalopathy-syndromes-in-infancy

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen